Request for Withdrawal of Final Office Action

Applicants respectfully request reconsideration and withdrawal of the finality of the Office Action dated June 22, 2001. The circumstances under which the finality of a second or subsequent Office Action are deemed proper are set forth in M.P.E.P. § 706.07(a) at 700-39, which provides in pertinent part:

> Under present practice, second or any subsequent actions on the merits shall be final, except where the examiner introduces a new ground of rejection that is neither necessitated by applicant's amendment of the claims nor based on information submitted in an information disclosure statement filed during the period set forth in 37 C.F.R. 1.97(c) with the fee set forth in 37 C.F.R. 1.17(p).

Applicants submit that the rejection of claims 36, 38-40, 42-44 and 48-50 under 35 U.S.C. § 103(a) encompasses a new ground of rejection that was not necessitated by Applicants' amendment of the claims. In particular, the Examiner introduced a new ground of rejection at page 3 of Paper No. 20, which could have been made previously but was not.

Claims 36, 38-40, 42-44 and 48-50 were rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Nair *et al.*, *J. Immunological Methods 152*:237-243 (1992) in view of Fearon *et al.*, *Cancer Res. 48*:2975-2980 (1988), Townsend *et al.*, *Cell 39*:13-25 (1984), Van Der Bruggen *et al.*, *Eur. J. Immunol. 24*:2134-2140 and "prior art disclosed in the specification (see page 3)." Paper No. 20, page 3.

These claims are drawn to tumor vaccines administered to a patient comprising tumor cells which have been charged with antigenic peptides. The amendments to claims 36 and 48 were made to paraphrase the terms of "act as ligand for" and "charged", and do not change the scope of the claims. Since the Examiner's new ground of rejection under 35 U.S.C. § 103(a)

is not based on any substantive change that resulted from the amendment of claims 36 and 48, this rejection could have been properly raised in the first Office Action (Paper No. 16). Thus, the new ground of rejection under 35 U.S.C. § 103(a) was not necessitated by Applicants' amendment. In addition, the Examiner's grounds for the new rejection under 35 U.S.C. § 103(a) were not based on information submitted in an information disclosure statement filed during the period set forth in 37 C.F.R. § 1.97(c) with the fee set forth in 37 C.F.R. § 1.17(p).

In view of the foregoing, it is respectfully submitted that the finality of the Office Action of June 22, 2001, is premature, and withdrawal of finality is respectfully requested.

Rejections under 35 U.S.C. § 102

The Examiner rejected claims 36, 38-40, 42-44 and 48-50 under 35 U.S.C. § 102(a) as allegedly being anticipated by Schmidt *et al.*, *Proc. Natl. Acad. Sci. USA 93*:9759-9763 (1996) and stated that this rejection can be overcome by supplying a certified English language translation of the foreign priority documents.

Applicants submit herewith a certified English language translation of German Application No. 195 43 649.0, filed November 23, 1995, and German Application No. 196 07 044.9, filed February 24, 1996. Support for claims 36, 38-40, 42-44 and 48-50 can be found, *inter alia*, at page 14, and pages 20-21 and the claims of the certified English translation of German Application No. 195 43 649.0. Accordingly, withdrawal of this rejection is respectfully requested.

Rejections under 35 U.S.C. § 103

The Examiner rejected claims 36, 38-40, 42-44 and 48-50 under 35 U.S.C. § 103(a) as allegedly being obvious over Nair *et al.*, *J. Immunological Methods 152*:237-243 (1992) in view of Fearon *et al.*, *Cancer Res. 48*:2975-2980 (1988), Townsend *et al.*, *Cell 39*:13-25 (1984), Van Der Bruggen *et al.*, *Eur. J. Immunol. 24*:2134-2140 and "prior art disclosed in the specification (see page 3)." Paper No. 20, page 3. Applicants respectfully traverse this rejection.

To establish a *prima facie* case of obviousness under 35 U.S.C. § 103, the Examiner must show that the prior art suggested to those of ordinary skill in the art that they should make the claimed composition or device, or carry out the claimed process, and that the invention could be attained with a reasonable expectation of success. See *In re Vaeck*, 20 U.S.P.Q.2d (BNA) 1438, 1442 (Fed. Cir. 1991). Any suggestion and reasonable expectation of success must come from the prior art of record, and not Applicants' disclosure. *Id.*

The Examiner stated that:

> Nair et al. disclose use of an organic polycation (e.g. cationic liposomes) to deliver an MHC class I antigen to tumor cells. Nair et al. teach that said method is an efficient means of sensitizing target cells for CTL lysis in the context of MHC class I.

Paper No. 20, page 3.

Nair *et al.* is directed to an antigen delivery system, the lipopoly-L-lysine. In Nair *et al.*, mice were injected with ovalbumin. In contrast, the instant claims are directed to a tumor vaccine wherein tumor **cells** are administered to a patient. Nothing in Nair *et al.* teaches or suggests administration of tumor cells to a living animal. Nair *et al.* does not teach or suggest

making a tumor vaccine comprising peptides and organic polycations. Furthermore, Nair *et al.* does not disclose tumor-bearing animal models. With respect to claim 44, as the Examiner expressly states, "Nair et al. do not disclose human tumor cells treated to express influenza virus peptide in the context of HLA class 1." (See Paper No. 20, page 3). Furthermore, Nair *et al.* disclose that "[t]he main contribution of LPLL-liposome would be as an in vitro antigen delivery system for studying antigen presentation." (See Nair *et al.*, page 242, last paragraph). Thus, Nair *et al.* actually teach away from the present invention, as Nair *et al.* state their system is useful for *in vitro* systems. Therefore, Nair *et al.* is deficient as a primary reference upon which to base a *prima facie* case of obviousness.

Fearon *et al.* is directed to transfection of murine colon carincoma cells with a gene encoding for the hemagluglutination antigen (HA) of influenza virus. In Fearon *et al.*, HA-transfected tumor cells were injected into mice. Nothing in Fearon *et al.* teaches or suggests making a tumor vaccine wherein the HA antigen is not transfected into the cells, but instead is incubated with the cells in the presence of organic polycation. Fearon *et al.* discloses transfection of **DNA** wherein the methods of the present invention are directed to incubation of **peptides**. There is no motivation to combine the disclosures of Nair *et al.* and Fearon *et al.*. Further, one of ordinary skill in the art would not have a reasonable expectation of success in combining Nair *et al.*'s *in vitro* antigen presenting system using peptides with Fearon's disclosed *in vivo* model using DNA transfected cells. In addition, none of the other art relied upon the Examiner (Townsend *et al.*, Van Der Bruggen *et al.*, or the prior art disclosed in the specification on page 3) cures the deficiency of Nair *et al.*

In the specification on page 3, those citations listed were said to "not [be] sufficiently immunogenic to trigger a cellular immune response which would be necessary to eliminate

tumor cells carrying tumor antigen; the co-administration of adjuvants provides only limited possibilities for intensifying the immune response." (See specification, page 3, lines 24-30). Townsend *et al.* is directed to the transfection of murine cells with hemagglutinin. Van Der Bruggen *et al.* is directed to a specific tumor antigen, MAGE-tumor antigen. None of the art relied upon the Examiner teaches or suggests modifying Nair *et al.* to arrive at the claimed invention. Specifically, none of the art suggests injecting the tumor cells disclosed in Nair *et al.* to patients in the form of a tumor vaccine. Therefore, there is no motivation to combine the references relied upon by the Examiner.

As previously stated, to establish a *prima facie* case of obviousness, there must be a reasonable expectation of success. See M.P.E.P. 2142. Combining the prior art relied upon the Examiner would not have been obvious nor would there be a reasonable expectation of success to combine the methods disclosed in the prior art to render the tumor vaccine of the present invention. Nair *et al.* is directed to *in vitro* methods of delivering antigens, not to *in vivo* methods. One of ordinary skill in the art would have no reasonable expectation of success to apply this particular *in vitro* method to an *in vivo* method.

The claims are not rendered obvious by any of the art relied upon by the Examiner. Accordingly, withdrawal of this rejection is respectfully requested.

Conclusion

All of the stated grounds of objection and rejection have been properly traversed, accommodated, or rendered moot. Applicants therefore respectfully request that the Examiner reconsider all currently outstanding objections and rejections and that they be withdrawn.

Applicants believe that a full and complete reply has been made to the outstanding Office Action and, as such, the present application is in condition for allowance. If the Examiner believes, for any reason, that personal communication will expedite prosecution of this application, the Examiner is invited to telephone the undersigned at the number provided.

Prompt and favorable consideration of this Reply is respectfully requested.

Respectfully submitted,

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